REMARKS

Claims 1-8 are all the claims pending in the application.

Claims 1, 2, 4, 5, 6 and 8 are amended herein.

New claims 11-22 are added herein to better define that which the Applicants consider their invention.

New claim 11 is supported in the specification at page 4, line 23.

New claims 12-13 are supported in the specification at page 4, lines 21-22, and page 5, ¶ 2.

New claims 14-15 are supported in the specification at page 5, ¶3.

New claims 16-22 are supported at page 5, ¶2.

New claims 20 and 21 are supported in the specification at page 6, ¶4.

New claim 22 is supported in the specification at pages 6-7.

No new matter is introduced within the meaning of 37 C.F.R. § 1.121(f). Entry of the amendments and new claims is requested.

Substitute Sequence Listing

Applicants submit herewith a replacement Sequence Listing in paper and computer readable form, and also required statements pursuant to 37 C.F.R. § 1.825(a) and (b).

In the previous Sequence Listing, filed on January 5, 2001, SEQ ID NO: 1 was inadvertently replaced with a duplicate copy of the sequence corresponding to SEQ ID NO: 5. SEQ ID NO: 1 is corrected in the replacement sequence listing, and corresponds to the open reading frame of SEQ ID NO: 3 (nucleotides 45-1295). The replacement SEQ ID NO:1 is

supported at pages 46-49 of the application as filed. In addition the final nucleotide number (1295) was omitted from the second occurrence of line <222> in SEQ ID NO: 3, and same is added in the replacement Sequence Listing. Support for this addition may be found at page 45, line 23, of the application as filed. No new matter is added, and entry of the substitute Sequence Listing is requested.

Claim Objections

Claims 1, 2, 4 and 5 are objected to as reciting the allegedly ungrammatical phrase "that comprising." Claims 1, 2, 4 and 5 are amended in accord with the Examiner's suggestion to substitute the word "comprises" for "comprising."

Claim 1 is amended to insert "A" at the start of the claim, as requested by the Examiner. Applicants assert that the remaining objection to claim 1 at paragraph 2.3 of the Office Action is rendered moot by deletion of the allegedly objectionable phrase in the present amendment to claim 1.

The objection to claim 6 under 37 C.F.R. § 1.75(c) for allegedly being in improper multiple dependent form is rendered moot by the present amendment, which amends claim 6 to depend only from claim 3.

Claim 8 is also objected to under 37 C.F.R. § 1.75(c) for allegedly being in improper multiple dependent form. This rejection is also rendered moot by the amendment to claim 8 herein, in which the two occurrences of "or 2" are deleted.

Applicants request that, in view of the amendments herein, these objections to claims 1-2, 4-6 and 8 be withdrawn.

Rejections under 35 U.S.C. §§ 101 and 112

(A) Claims 1-8 are rejected under 35 U.S.C. § 101 because the claimed invention allegedly lacks the support of either a specific and substantial asserted utility or a well established utility. A rejection under 35 U.S.C. § 112, ¶ 1, was also applied, on the grounds that, absent such utility, one of ordinary skill would not know how to use the claimed invention.

The rejected claims as amended herein are directed to polypeptides OAF065α and OAF065β, close homologues thererof, cDNAs encoding same, replication or expression vectors containing said cDNA, cells containing said vectors, and a method for producing said polypeptide.

Applicants respectfully traverse the rejection under 35 U.S.C. § 101, and thereby the related rejection under 35 U.S.C. § 112, on the grounds that a specific and substantial utility was asserted in the application as filed. In support of the utility asserted in the application as filed, Applicants submit herewith two references that support the utility taught in the specification.

Specifically, the specification and Figure 1 disclose that the sequence of the present invention comprises a cysteine-rich region. At page 4, lines 3-6, it is disclosed that the polypeptides of the type I membrane proteins, and that they have an extracellular cysteine-rich region that is common to the family of tumor necrosis factor receptors (TNFR, see Fig. 1 and page 39, lines 14-15). The 12 common cysteines are shown in Fig. 1. It is further disclosed (page 2, ¶ 2, and page 3, ¶ 2) that the peptides of the present invention were isolated on the basis of their expression in stromal cells in a form having a signal peptide that directs secretion from the cell, and that stromal cells were known to "produce and secrete essential factors to induce ... proliferation and differentiation of stem cells" (page 1, ¶ 3). Thus, Applicants assert that one of

ordinary skill of the art would have, upon reading the disclosure, immediately appreciated that the peptides of the present invention possessed utility based upon their membership of the TNFR family, by virtue of their source and their method of isolation, as having, for example, cell proliferating and cell differentiating activities (page 3, ¶ 2).

In support of the asserted utility, Applicants submit herewith a computerized analysis of the domain structure of the peptides of the present invention using the SMART program ("Simple Modular Architecture Research Tool," Schultz et al., 1998, *Proc. Natl. Acad. Sci. USA* 95:5857-5864; Schultz et al., 2000, Nuclei Acids Res. 28:231-234), which clearly identifies the proteins of the present invention as comprising TNFR domains (at Cys-34 to Cys-74, and Cys-75 to Cys-114) and therefore as being members of the TNFR family.

In further support of the cell proliferating and cell differentiating activities of the peptides of the present invention, Applicants submit herewith a second reference, which describes the cell proliferating and cell differentiating activities of the TNFR protein TAJ, which, for example, induces apoptosis via a mechanism that does not require either caspase or a "death domain" ("TAJ, a Novel Member of the Tumor Necrosis Factor Receptor Family, Activates the c-Jun N-terminal Kinase Pathway and Mediates Caspase-independent Cell Death" Michael T. Eby et al., 2000, *J. Biol. Chem.* 275:15336-15342, copy enclosed). The amino acid sequence of TAJ is substantially the same as polypeptide OFA065α of the present invention (see, Eby et al., Fig. 1A).

Thus, Applicants assert that the cell proliferating and cell differentiating activities of the present invention provide the required nexus between the diseases or disorders disclosed in the present application and the polypeptides of the present invention.

Applicants therefore assert that the invention of the rejected claims, as amended herein, is supported by a specific and substantial utility that was disclosed in the application as filed and is further supported by the two references submitted herewith. Therefore, Applicants request that the rejection under 35 U.S.C. § 101, and the related rejection under 35 U.S.C. § 112, ¶ 1, be withdrawn.

(B) Claims 1 and 3-8 are rejected under 35 U.S.C. § 112, ¶ 1, as allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors fully possessed the invention at the time of filing. Specifically it appears to be the Examiner's position that the two polypeptides, OAF065α and OAF065β, were not adequate to support the scope of a genus of polypeptides that included homologues having at least 70% homology to OAF065α or OAF065β over a region of at least 20 amino acids.

Applicants assert that the amendment to claim 1 herein renders this rejection moot. Claim 1, as amended, recites at least a polypeptide comprising the amino acid sequence shown in SEQ ID NO: 4 or 8, or comprising an amino acid sequence having at least 95% homology with the amino acid sequence shown in SEQ ID NO: 4 or 8. Thus, Applicants assert that the scope of the genus of claim 1 as amended is fully commensurate with the support afforded by

polypeptides OAF065α and OAF065β, which are two examples of the claimed genus that have entirely different C-terminal sequences.

Accordingly, Applicants request that the rejection of claims 1 and 3-8 under 35 U.S.C. § 112, ¶ 1, be withdrawn.

(C) Claims 1-8 are rejected under 35 U.S.C. § 112, ¶ 2, as being allegedly indefinite for comprising a broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation.

Applicants assert that this rejection is rendered moot by the amendment to claim 1 herein. Specifically, as amended, claim 1 no longer recites the language that was objected to, and clearly sets forth the metes and bounds of the invention. Thus, Applicants request that this rejection be withdrawn.

(D) Claims 4-8 are also rejected under 35 U.S.C. § 112, ¶ 2, as allegedly being indefinite for comprising a broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation.

Applicants assert that this rejection is rendered moot by the amendment to claims 4 and 5 herein, in which the phrase "or a fragment cDNA selectively hybridized to the cDNA" is deleted, and by the amendment to the dependency of claim 6. Applicants assert that, as amended, the rejected claims clearly set forth the metes and bounds of the invention. Thus, Applicants request that this rejection be withdrawn.

Rejections under 35 U.S.C. § 102

Claims 5-7 are rejected under 35 U.S.C. § 102(b) as being allegedly anticipated by Takeda, Database EST, Accession No. D82546.

Applicants assert that this rejection is rendered moot by the amendment to claim 5 herein. According to the Examiner, Takeda discloses 165 contiguous bases of SEQ ID NO: 2. Because the cDNA of claim 5 as amended may encompass a cDNA comprising SEQ ID NO:2, but does not encompass a fragment of cDNA that hybridizes to SEQ ID NO:2, Applicants assert that Takeda cannot anticipate any of claims 5-7. Accordingly Applicants request that this rejection be withdrawn.

Claims 3-7 are rejected under 35 U.S.C. § 102(b) as being allegedly anticipated by Hillier et al., Database EST, Accession No. W56629.

According to the Examiner, Hillier discloses a nucleic acid that is 99.7% identical to a 298 base pair region of SEQ ID NO: 1, which encodes a 98 amino acid portion of SEQ ID NO: 4.

Applicants assert that the amendments to claims 1, 4 and 5 herein render this rejection moot. Specifically, the polypeptide of claim 1 as amended may comprise the amino acid sequence SEQ ID NO: 4 or a close homologue thereof, but does not encompass a 98 amino acid portion of SEQ ID NO: 4. Thus, claim 3 is not anticipated by a nucleic acid that may be 99.7% identical to a 298 base pair region of SEQ ID NO: 1. Similarly, the cDNA of claims 5 and 6 is not anticipated by a nucleic acid that may be 99.7% identical to a 298 base pair region of SEQ ID NO: 1 because, as amended, these claims do not encompass cDNA fragments. Likewise, dependent claims 4 (as amended) and 7 are not anticipated.

Accordingly, Applicants request that this rejection be withdrawn.

Rejections under 35 U.S.C. § 103

Claims 1 and [sic, to] 8 are rejected under 35 U.S.C. § 103(a) as being allegedly obvious over either Takeda (as applied to claims 5-7), or Hillier, as applied to claims 3-7, in view of Sibson et al., WO 94/01548.

The Examiner cited Takeda and Hillier for the teaching of the DNA sequences as described above, and cites Sibson et al. as teaching that it is generally useful to place a desired cDNA sequence into an expression vector and host cell and to express the encoded protein.

Applicants assert that, for reasons given above in response to the rejections under 35 U.S.C. § 102(b), the claims as amended herein are not obvious over either Takeda or Hillier in view of Sibson.

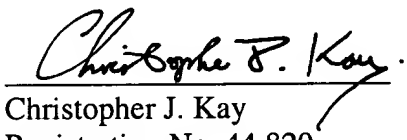
Specifically, neither Takeda nor Hillier teaches either the entire sequence of any cDNA that is encompassed by the claims as amended, or a cDNA encoding the entire amino acid sequence of any polypeptide sequence of the claims as amended. Thus, Takeda and Hillier either alone or in combination fail to teach or suggest all of the elements of the claimed invention as is required to make a *prima facie* case of obviousness. This deficiency is not cured by Sibson because Sibson does not teach either the amino acid or nucleic acid sequences of the claims as amended.

Accordingly, Applicants request that the rejection under 35 U.S.C. § 103(a) be withdrawn.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

Applicant hereby petitions for any extension of time which may be required to maintain the pendency of this case, and any required fee, except for the Issue Fee, for such extension is to be charged to Deposit Account No. 19-4880.

Respectfully submitted,



Christopher J. Kay
Registration No. 44,820

SUGHRUE MION, PLLC
2100 Pennsylvania Avenue, N.W.
Washington, D.C. 20037-3213
Telephone: (202) 293-7060
Facsimile: (202) 293-7860

Date: March 25, 2002

APPENDIX

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

The claims are amended as follows:

1. (amended) [Substantially] A substantially purified form of [the] a polypeptide [that comprising] that comprises the [amino-acid] amino acid sequence shown in SEQ ID [NO.] NO: 4 or 8, [homologue thereof, fragment thereof or homologue of the fragment] or that comprises an amino acid sequence having at least 95% homology with the amino acid sequence shown in SEQ ID NO: 4 or 8.

2. (amended) [A] The polypeptide according to claim 1 that [comprising] comprises the [amino-acid] amino acid sequence shown in SEQ ID [NO.] NO: 4 or 8.

4. (amended) [A] The cDNA according to claim 3 or 11 that [comprising] comprises the nucleotide sequence shown in SEQ ID [NO.] NO: 1 or 5 [or a fragment cDNA selectively hybridized to the cDNA].

5. (amended) [A] The cDNA according to claim 3 or 11 that [comprising] comprises the nucleotide sequence shown in SEQ ID [NO.] NO: 2 or 6 [or a fragment cDNA selectively hybridized to the cDNA].

6. (amended) A replication or expression vector carrying the cDNA according to claim 3 [to 5].

8. (amended) A method for producing the polypeptide according to claim 1 [or 2] which comprises culturing a host cell according to claim 7 under [a condition] conditions effective to express the polypeptide according to claim 1 [or 2].

Claims 11-27 are added as new claims.

11. (new) A cDNA encoding the polypeptide according to claim 2.

12. (new) A polypeptide in substantially purified form having the amino acid sequence of residues 1 to 392 of SEQ ID NO: 4.

13. (new) A polypeptide in substantially purified form having the amino acid sequence of residues 1 to 398 of SEQ ID NO: 8.

14. (new) A polypeptide in substantially purified form having an amino acid sequence that is at least 95% homologous with the amino acid sequence of residues 1 to 392 of SEQ ID NO: 4.

15. (new) A polypeptide in substantially purified form having an amino acid sequence that is at least 95% homologous with the amino acid sequence of residues 1 to 398 of SEQ ID NO: 8.

16. (new) A cDNA encoding a polypeptide according to claim 12.

17. (new) A cDNA encoding a polypeptide according to claim 13.

18. (new) A cDNA encoding a polypeptide according to claim 14.

19. (new) A cDNA encoding a polypeptide according to claim 15.

20. (new) A replication or expression vector comprising the cDNA according to claim 4.

21. (new) A replication or expression vector comprising the cDNA according to claim 5.

22. (new) A method for producing the polypeptide according to claim 2, which comprises culturing a host cell according to claim 7 under a condition effective to express the polypeptide according to claim 2.